ACTA SCIENTIARUM POLONORUM
Acta Sci. Pol., Technol. Aliment. 10(4) 2011, 507-513
ISSN 1644-0730 (print) ISSN 1889-9594 (online)

THE INFLUENCE OF SELECTED HYPOTENSIVE DRUGS ON THE BIOAVAILABILITY OF MINERALS FROM BUCKWHEAT GROATS IN VITRO ENZYMATIC DIGESTION

Joanna Sulibursk[1], Paweł Bogdański[2], Barbara Chiniewicz[1]
[1]Poznań University of Life Sciences
[2]University of Medical Science in Poznań

Background. The mineral status in hypertensive patients may be affected by hypotensive drugs. The aim of this study was to estimate the influence of hypotensive drugs (angiotensine converting enzyme inhibitors (ACE-I), β-blockers, Ca-antagonists, diuretics) on the potential bioavailability of magnesium, iron, zinc and copper from buckwheat groats in vitro enzymatic digestion.
Material and methods. The degree of release of magnesium, iron, zinc and copper from buckwheat groats was determined with and without (the control sample) an addition of hypotensive drugs. Four antihypertensive drugs in one dose (one tablet per sample) were analysed: metocard (a β-blocker), cardilopin (a Ca-antagonist), apo-perindox (ACE-I) and indapen (a diuretic). The samples were subjected to enzymatic digestion under in vitro conditions. The content of minerals in buckwheat groats before and after enzymatic digestion was determined by flame atomic absorption spectrometry (AAS).
Results. It was found that cardilopin (amlodipine) and indapen (indapamide) significantly increased the release of zinc from groats. The degree of release of magnesium was higher and the release of iron was lower in samples with apo-perindox (perindopril) than in the control group. The release of copper was significantly decreased by indapen (indapamid).
Conclusions. Amlodipine, perindopril and indapamide affected the release of magnesium, iron, zinc and copper from buckwheat groats in vitro enzymatic digestion.

Key words: food-drug interaction, minerals bioavailability

Corresponding author – Adres do korespondencji: Dr n. farm. Joanna Sulibursk, Department of Hygiene and Human Nutrition of Poznań University of Life Sciences, Wojska Polskiego 31, 60-624 Poznan, Poland, e-mail: jsulibur@up.poznan.pl

INTRODUCTION

In our previous study mineral status disorders were observed in patients with hypertension [Suliburska et al. 2011]. There are many factors that influence mineral absorption, excretion and metabolism. In vitro and in vivo studies showed that bioavailability of minerals depends on the content of various antinutrients in food, such as oxalic acid, phytates, dietary fibres and polyphenols, that act as mineral binders or chelators [Oatway et al. 2001, Sandberg 2002]. The degree of mineral release from food products depends also on the technological processing applied [Suliburska et al. 2009 a].

The mineral status in hypertensive patients may also be affected by hypotensive drugs. Loop diuretics can cause hypercalcuria and hypermagnesuria and bone loss [Law et al. 2005]. Treatment with ACE-I and loop diuretics results in a decrease in the serum concentration of magnesium and high losses of this element with urine. However, it was also shown that lisinopril is magnesium-sparing in patients with congestive heart failure [Oladapo and Falase 2000]. It was found that thiazides has a beneficial effect on calcium metabolism in elderly persons [Ott et al. 2008]. Golic et al. [1998] found that treatment of hypertensive patients using captopril or enalapril may result in zinc deficiency.

An interaction of antihypertensive drugs with minerals can occur in the digestive tract of patients at the stage of digestion. The aim of this study was to estimate the influence of hypotensive drugs on the bioavailability of magnesium, iron, zinc and copper from buckwheat groats in vitro enzymatic digestion.

MATERIAL AND METHODS

Food sample

The experimental material was buckwheat groats, purchased from the local market (the city of Poznan, 2010). Food samples were ground under laboratory conditions with an electrical mill and divided using appropriate sieves into fractions with particles having maximum diameters below 2 mm. Samples were dried at 105°C.

Drugs

In the experiment four antihypertensive drugs were used: metocard (a β-blocker), cardilopin (a Ca-antagonist), apo-Perindox (ACE-I) and indapen (a diuretic). Characteristics of the drugs are shown in Table 1.

Table 1. Characteristics of the drugs

Drug	Active substance	Dose of active substance mg/1 tablet	Antihypertensive--drug class
Metocard	metoprolol	47.5	β-bocker
Cardilopin	amlodipine	10	Ca-antagonist
Apo-Perindox	perindopril	3.34	ACE inhibitor
Indapen	indapamide	1.5	diuretic

Enzymatic digestion

Samples were divided with five groups: control, metocard, cardilopin, apo-perindox and indapen. The control samples comprised only the product without any drugs. One tablet of a given analyzed drug was added to each of the other samples.

In vitro enzymatic digestion was performed according to the method developed by Skibniewska et al. [2002]. In the experiment one dose of each drug (equivalent of 1 tablet) was analyzed. Tablets were crushed in a mortar. Each tablet of a given drug was mixed with a sample (2 g) of finely ground buckwheat groats in conical beakers, treated with deionised water (20 ml) and shaken for 10 min. In order to create suitable conditions for pepsin action, pH was brought to 2 using 0.1M HCl aqueous solution (Suprapure, Merck) and then pepsin solution (0.5 ml/100 ml) was added to the homogenate. Subsequently samples were placed in a thermostat shaker (37°C) for 2 hours. During the incubation process pH was assured or corrected by an addition of 6M HCl aqueous solution, when necessary. After 2 hours digested samples were treated with 6% $NaHCO_3$ aqueous solution (Extrapure, Merck) to bring pH to 6.8-7.0, subjected to pancreatin solution (10 ml/40 ml of homogenate), and placed in a thermostatic shaker (37°C) for 4 hours. Afterwards, digested samples were centrifuged for 10 min (3.800 rpm/min), and a clear solution was quantitatively transferred to quartz crucibles, and treated with a mixture of concentrated nitric (65% w/w) and perchloric (70% w/w) acids (2:1 v/v) (Suprapure, Merck). Samples were placed in a thermostatic block and heated until complete mineralization.

Control samples were also prepared, in which the product was digested without any addition of the drugs. For each drug a reagent sample was also prepared, which contained one tablet of a given drug and reagents. All samples were subjected to the process of enzymatic digestion.

In order to determine the total content of minerals in native products, food samples (2 g) were ashed in a muffle furnace at 450°C until complete mineralization and then dissolved in 1N nitric acid.

All samples were analysed in triplicate.

Determination of minerals

The content of minerals in native in vitro digested food products (with or without drugs) was determined by atomic absorption spectrometry (AAS-3, Zeiss spectrometer), after an appropriate dilution with deionized water (for Fe, Zn, Cu) or with $LaCl_3$ (0.3% solution, for Mg) using the air-acetylene flame. The methods were validated by a simultaneous analysis of the reference material (*Soya Bean Flour, INCT-SBF-4*), with the accuracy for Mg, Fe, Zn and Cu of 93.1%, 97.2%, 94.5% and103.1%, respectively. The content of minerals in food products was expressed in mg/100 g dry mass, while the degree of a mineral release (potential bioavailability) was expressed as a percentage of the mineral released *vs.* its total content.

Statistical analysis

The experimental results were given as means ±SD of three parallel measurements. The statistical analysis was carried out using the STATISTICA 7.0 software and the ANOVA test was performed at the significance level $\alpha = 0.05$.

RESULTS

Table 2 shows the total content of minerals in the buckwheat groats. This table also presents the amount of minerals (mg) released from 100 g of products (the control sample). This index may reflect their potential bioavailability.

Table 2. Content of minerals and their release in buckwheat groats

Parameters mg/100 g d.w.	Mg	Fe	Zn	Cu
Content of minerals	155.9 ±2.15	2.45 ±0.02	5.17 ±0.09	0.52 ±0.01
Released minerals	69.9 ±1.15	0.34 ±0.01	0.86 ±0.02	0.40 ±0.01

Table 3 presents the degree of release of minerals in the samples with or without drugs. As it can be seen, in some cases the analysed drugs affected the degree of release of minerals from groats. It was found that apo-perindox caused a markedly higher release of magnesium, but a lower release of iron from buckwheat groats when compared with the control sample. The amount of available zinc was significantly higher in samples with cardilopin and indapen than in the samples without any drugs. Moreover, indapen markedly reduced the release of copper from the product. However, metocard did not significantly affect the degree of release of minerals from the groats.

Table 3. The degree of release of minerals according to the analysed drugs

Samples	Mg %		Fe %		Zn %		Cu %	
Control	44.9 ±1.88^{ab}	–	14.0 ±0.74^{b}	–	16.5 ±0.66^{a}	–	76.1 ±1.23^{bc}	–
Metocard (β-bloker)	40.8 ±2.21^{a}	(–)9.05*	15.7 ±0.03^{b}	(+)12.1*	17.5 ±0.42^{a}	(+)5.92*	65.1 ±0.43^{b}	(–)14.5*
Cardilopin (Ca-antagonist)	49.0 ±0.14^{cb}	(+)9.32*	16.4 ±0.18^{b}	(+)17.1*	26.0 ±0.08^{b}	(+)57.3*	80.2 ±0.11^{c}	(+)5.43*
Apo-Perindox (ACE-inhibitor)	53.5 ±0.85^{c}	(+)19.3*	7.69 ±0.35^{a}	(–)45.1*	17.5 ±0.34^{a}	(+)6.13*	81.9 ±0.78^{c}	(+)7.65*
Indapen (diuretic)	44.6 ±0.79^{ab}	(–)0.53*	16.5 ±0.61^{b}	(+)17.7*	25.7 ±1.12^{b}	(+)55.5*	33.1 ±1.14^{a}	(–)56.6*

*+/– – degree of released minerals in comparison with control sample.
$^{a, b, c}$ – significant differences, $p < 0.05$.

DISCUSSION

Drugs are various chemical compounds that may interact with food. These interactions can lead to a reduced or increased release of minerals from food and it may affects the bioavailability of minerals.

It is known that ACE inhibitors, such as captopril and enalapril, have functional groups such as sulphydryl groups or carboxyl groups and the ability of these groups to bind zinc determines the mineral status of the organism [Golik et al. 1998]. Angiotensin converting enzyme inhibitors bind metal ions (iron, copper and zinc) and by this mechanism drugs may interfere with metal-catalyzed reactions (free radical generation), or metal absorption and excretion [Fernandes et al. 1996, Leary et al. 1992]. Fernandez et al. [1998] showed the ability of the ACE inhibitors (captopril, enalapril, lisinopril) to bind iron and copper and they also suggested that copper was more effective than iron in the formation of metal-drug complexes. Moreover, Haenni et al. [1997] observed that treatment of hypertensive patients with an ACE inhibitor (fosinopril) was related to an alternation in their calcium and magnesium status. In that study the reduction in serum ACE activity correlated with an increase in magnesium serum concentration and a decrease in the Ca/Mg ratio in the serum. In this study perindopril markedly affected the release of magnesium and iron from buckwheat groats. It may have been caused by the formation of insoluble complexes between drug and iron ions. Moreover, the effect of the drug interaction with food components may have increased the release of magnesium ions from the chemical bonds.

In this study metaprolol was not found to interact with minerals. However, another β-blocker – carvedilol – is a metal chelator and exhibits antioxidant activity [Oettl et al. 2001]. It was also found that propranolol (a β-blocker) and verapamil (a Ca-antagonist) have a significant inhibitory effect on peroxidation in the tissues in the presence of iron ions [Aruoma et al. 1991].

It is known that indapamid forms complexes with copper under appropriate conditions [Radi 2003]. Under in vitro digestion conditions applied in this study it was observed that indapamid resulted in a significant decrease of the release of copper from groats.

In our previous study we found that amlodipin and indapamid markedly affected the increase in pepsin activity [Sulibursk a et al. 2009 b]. The increase in the activity of digestive enzymes can cause a greater release of minerals from complexes with other components of buckwheat. It was observed that both cardilopin (amlodipine) and indapen (indapamid) significantly increased the release of zinc from the product.

CONCLUSIONS

1. Amlodipine, perindopril and indapamide affected the release of magnesium, iron, zinc and copper from buckwheat groats in vitro enzymatic digestion.
2. Hypotensive drugs may influence potential bioavailability of minerals.

REFERENCES

Aruoma O.I., Smith Ch., Cecchini R., Evans P.J., Halliwell B., 1991. Free radical scavenging and inhibition of lipid peroxidation by β-blockers and by agents that interfere with calcium metabolism: A physiologically-significant process? Biochem. Pharm. 42, 4, 735-743.

Fernandes A.C., Filipe P.M., Freitas J.P., Manso C.F., 1996. Different effects of thiol and non thiol ACE inhibitors on copper induced lipid and protein oxidative modification. FRBM 20, 4, 507-514.

Fernandez M.T., Silva M.M., Mira L., Florencio M.H., Gill A., Jennings K.R., 1998. Iron and copper complexation by angiotensin-converting enzyme inhibitors. A study by ultraviolet spectroscopy and electrospray mass spectrometry. J. Inorg. Biochem. 71, 93-98.

Golik A., Zaidenstein R., Dishi V., Blatt A., Cohen N., Cotter G., Berman S., Weissgarten J., 1998. Effects of captopril and enalapril on zinc metabolism in hypertensive patients. J. Am. Coll. Nutr. 17, 1, 75-78.

Haenni A., Berglund L., Reneland R., Anderssson P., Lind L., Lithell H., 1997. The alterations in insulin sensitivity during angiotensin converting enzyme inhibitor treatment are related to changes in the calcium/magnesium balance. Am. J. Hyper. 10, 2, 145-151.

Law P.H., Sun Y., Bhattacharya S.K., Chhokar V.S., Weber K.T., 2005. Diuretics and bone loss in rats with aldosteronism. J. Am. Coll. Cardiol. 46, 1, 142-146.

Leary W.P., Phil D., Reyes A.J., van der Bryl K., 1992. Effects of angiotensin-converting enzyme inhibitors on urinary excretions: interactions with diuretics. Am. J. Med. 92, 4, 64-68.

Oatway L., Vasanthan T., Helm J.H., 2001. Phytic acid. Food Rev. Inter. 17, 419-431.

Oettl K., Greilberger J., Zangger K., Haslinger E., Reibnegger G., Jurgens G., 2001. Radical--scavenging and iron-chelating properties of carvedilol an antihypertensive drug with antioxidative activity. Biochem. Pharmacol. 62, 241-248.

Oladapo O.O., Falase A.O., 2000. Serum and urinary magnesium during treatment of patients with chronic congestive heart failure. Afr. J. Med. Med. Sci. 29, 3-4, 301-303.

Ott S.M., LaCroix A.Z., Scholes D., Ichikawa L.E., Wu K., 2008. Effects of three years of low--dose thiazides on mineral metabolism in healthy elderly persons. Osteoporos Int. 19, 9, 1315--1322.

Radi A., 2003. Adsorptive cathodic stripping voltammetric determination of indapamide as copper complex at a hanging mercury drop electrode. Chem. Anal. 48, 2, 273-281.

Sandberg A.S., 2002. Bioavailability of minerals in legumes. Br. J. Nutr. 88, S281-S285.

Skibniewska K., Kozirok W., Fornal L., Markiewicz K., 2002. In vivo availability of minerals from oat products. J. Sci. Food Agric. 82, 1676-1681.

Suliburska J., Bogdański P., Krejpcio Z., Pupek-Musialik D., 2009 a. The influence of perindopril, amlodipine and indapamide on pepsin activity in vitro. Farm. Współ. 2, 171-174.

Suliburska J., Krejpcio Z., Lampart-Szczapa E., Wójciak R.W., 2009 b. Effect of fermentation and extrusion on the release of selected minerals from lupine grain preparations. Acta Sci. Pol., Technol. Aliment. 8, 3, 87-96.

Suliburska J., Bogdański P., Pupek-Musialik D., Krejpcio Z., 2011. Dietary intake and serum and hair concentrations of minerals and their relationship with serum lipids and glucose levels in hypertensive and obese patients with insulin resistance. Biol. Trace Elem. Biol. 139, 137-150.

WPŁYW WYBRANYCH LEKÓW HIPOTENSYJNYCH NA BIODOSTĘPNOŚĆ SKŁADNIKÓW MINERALNYCH Z KASZY GRYCZANEJ W PROCESIE TRAWIENIA IN VITRO

Wstęp. Leki hipotensyjne mogą mieć wpływ na stan odżywienia mineralnego pacjentów z nadciśnieniem tętniczym. Celem badań było określenie wpływu leków hipotensyjnych (inhibitory konwertazy angiotensyny (ACE-I), β-blokery, antagoniści kanałów wapniowych, diuretyki) na potencjalną biodostępność magnezu, żelaza, cynku i miedzi z kaszy gryczanej w warunkach trawienia enzymatycznego in vitro.

Materiał i metody. Stopień uwolnienia magnezu, żelaza, cynku i miedzi z kaszy gryczanej określany był w próbkach z dodatkiem i bez dodatku (próbka kontrolna) leków hipotensyjnych. Analizowano cztery leki przeciwnadciśnieniowe w jednej dawce (jedna tabletka w próbce): metocard (β-bloker), cardilopin (antagonista kanałów wapniowych),

apo-perindox (ACE-I) i indapen (diuretyk). Próbki poddano trawieniu enzymatycznemu w warunkach in vitro. Zawartość składników mineralnych w kaszy gryczanej przed i po trawieniu enzymatycznym określono z użyciem płomieniowej absorpcyjnej spektrometrii atomowej (AAS).
Wyniki. Stwierdzono, że cardilopin (amlodypina) i indapen (indapamid) istotnie zwiększały uwalnianie cynku z kaszy. W porównaniu z grupą kontrolną stopień uwolnienia magnezu był wyższy, a żelaza niższy w próbkach z apo-perindox (perindopril). Indapen (indapamid) znacząco obniżył uwalnianie miedzi.
Wnioski. Amlodypina, perindopril i indapamid wpływają na uwalnianie magnezu, żelaza, cynku i miedzi z kaszy gryczanej w warunkach trawienia in vitro.

Słowa kluczowe: interakcje lek-żywność, biodostępność składników mineralnych

Received – Przyjęto: 17.06.2011

Accepted for print – Zaakceptowano do druku: 12.09.2011

For citation – Do cytowania: Suliburska J., Bogdański P., Chiniewicz B., 2011. The influence of selected hypotensive drugs on the bioavailability of minerals from buckwheat groats in vitro enzymatic digestion. Acta Sci. Pol., Technol. Aliment. 10(4), 507-513.